Nasopharyngeal Carriage Rate and Susceptibility of *Haemophilus influenzae* to Antimicrobials in Central Part of Russia

Poster No.: P0581

O. KRETCHIKOVA, G. RESHEDKO, O. STETSIOUK, O . EGOROVA, T. BOGDANOVICH, L. STRATCHOUNSKI

Department of Clinical Pharmacology and Antimicrobial Chemotherapy, Smolensk State Medical Academy, Smolensk, Russia

Tel: +7-0812-553401, 552327
Fax: +7-0812- 552327
Email: root@cliph.keytown.com

ABSTRACT

Objectives: To evaluate the rate of nasopharyngeal carriage of *Haemophilus influenzae* (Hif) among the children of 1-6 years old from the day-care centres in central region of Russia and to elucidate the current resistance patterns of Hif.

Methods: A total of 733 children from Moscow, Smolensk and Yartstevo were included into this study. Nasopharyngeal cultures were collected using sterile cotton swabs. Isolates were identified with Gram stain, oxidase, X+V factors. MICs were determined with Etests method. Agents tested were ampicillin (AM), amoxicillin/clavulanate (XL), cefaclor (CF), erythromycin (ER), clarithromycin (CH), roxithromycin (RO) and co-trimoxazole (TS). β-lactamase testing was performed with nitrocefin. Quality control was performed using *H.influenzae* ATCC 49247 and ATCC 49766.

Results: A total nasopharyngeal carriage rate of Hif was 44%, varying from 32% in Moscow to 46% and 55% in Yartstevo and Smolensk respectively. Only 2% of the strains were resistant to AM and 0.6% to XL and CF. Of 3 AM-resistant strains 1 strain was β-lactamase-positive. Both ER and RO demonstrated very low activity against Hif (R%/I% were 12/88 and 97.9/2.1 respectively). The CH-resistance rate was 18.7%. The highest level of resistance registered was for TS (20.9%).

Conclusion: There is a low prevalence of both β-lactamase-positive and β-lactamase-negative AM-resistant strains in children from central part of Russia. AM remains the drug of choice for treatment of Hif infections. However, it is necessary to continue surveillance of AM-resistance in regions participated. Of all tested macrolides only CH had notable activity against Hif.

INTRODUCTION AND PURPOSE

H.influenzae causes various infections. Data obtained from various studies have demonstrated that antibiotic resistance in *H.influenzae* had reached epidemic proportions and varies greatly in different regions of the world. Nasopharyngeal colonisation of children reflects the strains currently circulating in the community and causing infections.

The purpose of the study was to investigate the carriage rate and the susceptibility of nasopharyngeal strains of *H.influenzae* to β-lactams, macrolides and co-trimoxazole.

MATERIALS AND METHODS

Nasopharyngeal strains of *H.influenzae* were collected during 1997 from healthy children attending day-care centers in Moscow, Smolensk and Yartstevo. Isolation and identification were done according standard methods. Susceptibility testing was done with E-tests (AB Biodisk, Sweden). The antibiotics tested were ampicillin (AM), amoxicillin/clavulanate (XL), cefaclor (CF), erythromycin (ER), clarithromycin (CH), roxithromycin (RO) and co-trimoxazole (TS). *H.influenzae* strains were tested on Haemophilus Test Medium (Oxoid, UK), inoculum 0.5 McFarland, incubation for 16-18 h at 35°C with 5% CO_2. *H.influenzae* ATCC 49247 and 49766 strains were used for quality control. Interpretation of susceptibility results was performed according to criteria of NCCLS-97 (USA) for β-lactams, clarithromycin and co-trimoxazole and SFM-96 (France) for erythromycin and roxithromycin. Data were calculated using software M-Lab.

RESULTS AND DISCUSSION

A total of 733 children were included into this study. The nasopharyngeal carriage rate of *H.influenzae* was 44% varying from 32% in Moscow to 55% and 46% in Smolensk and Yartstevo respectively. In total 323 *H.influenzae* strains were isolated, 300 from these were tested to the studied antimicrobials. The antimicrobial activity of tested drugs against nasopharyngeal isolates of *H.influenzae* are indicated in the following table.

Table. The *in-vitro* activity of antimicrobials against nasopharyngeal strains of *H.influenzae*

Antimicrobials	Breakpoints S	Breakpoints R	N of strains	%R	%I	%S	MIC_{50}	MIC_{90}	MIC Range
Ampicillin	≤ 1	≥ 4	300	0,9	1,2	97,9	0,19	0,38	0,016-128
Amoxicillin/clavulanate	≤ 4/2	≥ 8/4	300	0,6	0	99,4	0,5	1	0,016-8
Cefaclor	≤ 8	≥ 32	300	0,6	0	99,4	1	3	0,25-32
Erythromycin	≤ 1	> 4	300	12,0	88,0	0	4	8	1-16
Clarithromycin	≤ 8	≥ 32	300	0	18,7	81,3	6	12	1-24
Roxithromycin	≤ 1	> 4	300	97,9	2,1	0	16	32	4-128
Co-trimoxazole	≤ 0,5/9,5	≥ 4/76	300	20,3	0,6	79,1	0,125	32	0,016-32

Only 2,1% of the tested strains were resistant to ampicillin (including R and I) and 0.6% to amoxicillin/clavulanate and cefaclor. Only one of the 3 ampicillin-resistant strains was β-lactamase-positive (nitrocefin test) and susceptible to amoxicillin/clavulanate and cefaclor. The level of β-lactamase-production in strains isolated in our study (0,3%) was significantly lower than in United States (19,7-37,9%) and in Eastern Europe (9,0-19,5%) (Doern *et al.*, 1996).

The other two resistant strains were β-lactamase-negative ampicillin-resistant (BLNAR) and resistant to amoxicillin/clavulanate and cefaclor what may be due to the production of altered forms of penicillin-binding proteins or decreased permeability of the cell wall. It is worth to note that ampicillin-resistant (R) strains were isolated only in Smolensk, all strains from Yartstevo were ampicillin-susceptible.

Both erythromycin and roxithromycin demonstrated very low *in vitro* activity against *H.influenzae* (R%/I% were 12,0/88,0 and 97,9/2,1 respectively). However most strains had intermediate level of resistance to erythromycin with MIC_{50}/MIC_{90} - 4/8 mg/L. The clarithromycin resistance rate was 18.7%, despite MIC_{50}/MIC_{90} of this drug were some higher than of erythromycin (6/12 mg/L).

The highest level of resistance was registered for co-trimoxazole (20.9%). That exceeds the rates reported in European countries (0-12%) and United States (0-4.3%) (Doern *et al.*, 1996). Probably the high rate of co-trimoxazole resistance is due to frequent administration of the drug in ambulatory practice in Russia.

CONCLUSIONS

- The low prevalence of both β-lactamase-positive and BLNAR nasopharyngeal isolates of *H.influenzae* suggests that aminopenicillins remain the drugs of choice for the treatment of infections caused by *H.influenzae* in central part of Russia.
- Of all tested macrolides only clarithromycin has notable activity against *H.influenzae*.
- Co-trimoxazole probably should be avoided as the drug of empirical choice because of high prevalence of resistant strains.